IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

1632

In the Application of GLENN et al.

Atty Dkt. 4057-25
C# M#

Serial No. 09/311,720

Group Art Unit: 1632

Examiner: J.T. Woitach

Filed: May 14, 1999

Date: April 23, 2003

Title: GENETIC IMMUNIZATION BY EPICUTANEOUS APPLICATION

OIPE JC154 APR 23 2003 PATENT & TRADEMARK OFFICE

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Assistant Commissioner for Patents
Washington, DC 20231

Sir:

AMENDMENT UNDER 37 CFR §1.111

This is a response/amendment/letter in the above-identified application and includes an attachment which is hereby incorporated by reference and the signature below serves as the signature to the attachment in the absence of any other signature thereon.

☒ **Correspondence Address Indication Form Attached.**

Fees are attached as calculated below:

Total effective claims after amendment **0** minus highest number previously paid for **20** (at least 20) = 0 x $ 18.00	$	0.00
Independent claims after amendment **0** minus highest number previously paid for **3** (at least 3) = 0 x $ 84.00	$	0.00
If proper multiple dependent claims now added for first time, add $280.00 (ignore improper)	$	0.00
Petition is hereby made to extend the current due date so as to cover the filing date of this paper and attachment(s) ($110.00/1 month; $410.00/2 months; $930.00/3 months)	$	930.00
Terminal disclaimer enclosed, add $ 110.00	$	0.00
☐ First/second submission after Final Rejection pursuant to 37 CFR 1.129(a) ($750.00) ☐ Please enter the previously unentered , filed ☐ Submission attached	$	0.00
Subtotal	$	**930.00**
If "small entity," then enter half (1/2) of subtotal and subtract ☐ Applicant claims "small entity" status. ☐ Statement filed herewith	-$	0.00
Rule 56 Information Disclosure Statement Filing Fee ($180.00)	$	0.00
Assignment Recording Fee ($40.00)	$	0.00
Other:		**0.00**
TOTAL FEE ENCLOSED	$	**930.00**

The Commissioner is hereby authorized to charge any deficiency, or credit any overpayment, in the fee(s) filed, or asserted to be filed, or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Account No. 14-1140. A duplicate copy of this sheet is attached.

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NIXON & VANDERHYE P.C.
By Atty: Gary R. Tanigawa, Reg. No. 43,180

Signature: _____

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

GLENN et al.

Atty. Ref.: 4057-25

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FOR: GENETIC IMMUNIZATION BY EPICUTANEOUS APPLICATION

* * *

RESPONSE UNDER 37 CFR § 1.111

April 23, 2003

Hon. Commissioner for Patents
Washington, D.C. 20231

Sir:

In response to the pending Office Action (Paper No. 22) mailed October 23, 2002, reconsideration and allowance are respectfully requested.

Claims 1-127 are pending.

In the present application, support for the claimed invention can be found in original claims 45-46, 69 and 73-74; page 14, lines 1-12, and page 36, line 16, to page 37, line 12, of the specification; Examples 19, 34 and 38. The skin can be intact for genetic immunization, or exposed to the epidermal layer using a chemical or mechanical penetration enhancer. See page 7, lines 2-13 and 20-23; page 8, lines 7-12; and page 124, lines 15-17, of the specification. With the mouse model used in the examples, the fur/hair is generally shaved prior to transcutaneous immunization. But hair-containing skin can also be used as described on page 18, line 8-9, and page 79, line 3, of the specification. For example, where fur/hair would not prevent application of the immunization solution (cf. the ear of a mouse or the arm of a human volunteer to the shaved dorsum on page 40, lines 4-5, of the specification), removal of the fur/hair from the skin prior to transcutaneous immunization would not be necessary.

On page 2 of Paper No. 22, the Examiner acknowledged Applicants' request for an interference with U.S. Patent 6,087,341. Note that on March 14, 2002, Applicants also requested an interference with U.S. Patent 6,348,450. It is understood that these requests will be considered after allowable claims have been identified. Applicants

would be the senior party in those interferences because the present claims are entitled to at least an earlier priority date of November 14, 1996 (i.e., the effective filing date of this application).

Election/Restriction

Applicants acknowledge consideration by the Examiner of their traversal of the restriction requirement. Upon an indication that a generic or linking claim is allowable, rejoinder of withdrawn claims is requested.

Priority

On page 2 of Paper No. 22, the Examiner states the priority claim from the Official filing receipt. But this is incorrect and Applicants requested correction on February 28, 2000 (the cover sheet submitted on May 14, 1999 and the Rule 63 Declaration submitted on November 15, 1999 show the correct priority claim). The first paragraph of the specification describing the relationship among the parent applications was last amended on July 10, 2001; a substitute Rule 63 Declaration was submitted on November 5, 2001. The Official filing receipt mailed on April 3, 2002 failed to correct the "Domestic Priority" section in accordance with Applicant's priority claim. All of the four nonprovisional U.S. applications, the PCT application designating the U.S., and the provisional U.S. application were still pending when this application was filed. Therefore, this application is a continuation in-part of the five nonprovisional applications and it claims priority benefit of the provisional application.

On page 5 of Paper No. 22, it was stated, "upon review of the parental continuation in part applications listed in the priority statement, specific support for the elected subject matter presently under examination is not found." In particular, the Examiner asserts that support for the elected species of sequestrin is first found in this application.

Compliance with the requirements of the first paragraph of 35 U.S.C. § 120 is shown by the disclosures filed on November 14, 1996 (U.S. Appln. 08/749,164 issued as U.S. Patent 5,910,306); July 17, 1997 (U.S. Appln. 08/896,085 issued as U.S. Patent 5,980,898); and November 14, 1997 (Intl. Appln. PCT/US97/21324 and WO 98/20734).

For ease of reference, this description will be cited according to the column and line of the U.S. patents and the published PCT application (see attached copies). As shown below, support for the invention as broadly claimed in the independent claims shows that Applicants were in possession of the invention prior to May 21, 1998.

Transcutaneous immunization by epicutaneous application of antigen (e.g., a gene product) was first described in U.S. Appln. 08/749,164 filed on November 14, 1996. In particular, antigen is described on cols. 5-6 of the '306 patent. In particular, col. 5, lines 62-63, of the '306 patent teaches that antigen may be expressed by recombinant technology. Plasmodium is listed as a source for antigen on col. 6, line 54, of the '306 patent. Such support is sufficient to satisfy Section 112, first paragraph, for at least the broad scope of the invention (e.g., independent claims 1, 80, 93, 102, 110, 112 and 115). It is submitted that such claims, inter alia, are specifically supported by the specification of U.S. Appln. 08/749,164 because compliance with the requirements of the Patent Act is determined on a claim-by-claim basis.

Genetic immunization by epicutaneous application of polynucleotide (providing antigen and/or adjuvant using nucleic acid) is also described in U.S. Appln. 08/896,085 (see col. 4, lines 24-28, and col. 14, lines 13-29, of U.S. Patent 5,980,898). Sequestrin antigen provided as nucleic acid (Example 19) or protein (Example 20) is shown to be successfully used in transcutaneous immunization on pages 62-65 of WO 98/20734. These teachings are repeated in the present specification.

It is respectfully submitted that the Examiner acknowledge that Applicants have complied with the requirements of 35 U.S.C. §§ 119(e) and 120 to receive benefit of an earlier filing date of November 14, 1996 (i.e., the filing date of U.S. Appln. 08/749,164). A corrected Official filing receipt should be mailed.

Information Disclosure Statement

The Examiner objected to the previously filed Information Disclosure Statement (IDS). In response, another IDS including the documents listed therein on Forms PTO-1449 was submitted on April 8, 2003. The Examiner's consideration of those documents and return of the initialed Forms PTO-1449 are requested.

Claim Objections

Claims 1, 80, 93, 102, 110 112, 115 and 117 were objected to and the Examiner suggested amending the independent claims to reflect the elected invention. With regard to the elected invention (i.e., Applicants' response to the restriction requirement), it is submitted that a generic claim is consistent with the election made on March 14, 2002. Applicants have also elected species i) sequestrin, ii) CpG1, and iii) adenoviral regulatory region. This species election does not require amendment of the claims.

Applicants request withdrawal of the claim objections.

35 U.S.C. 112 – Enablement

The Patent Office has the initial burden to question the enablement provided for the claimed invention. M.P.E.P. § 2164.04, and the cases cited therein. It is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. *In re Marzocchi*, 169 USPQ 367, 370 (C.C.P.A. 1971). Specific technical reasons are always required. See M.P.E.P. § 2164.04.

Claims 1-31, 35-36, 39-41, 44-46, 55-58, 72 and 75-127 were rejected under Section 112, first paragraph, because it was alleged that the specification "does not reasonably provide enablement for a method of immunization." Applicants traverse.

It was found on page 7 of Paper No. 22 that the specification was enabling for "a method of inducing an immune response in a mammal comprising the steps: providing a polynucleotide construct comprising adenoviral regulatory region operatively linked to a polynucleotide; administering said construct to a mammal wherein administration results in the expression of said construct and production of a sequestrin polypeptide and induces an immune response in said mammal to said encoded sequestrin" (page 7 of Paper No. 22). Applicants submit that this finding is inconsistent with the assertion that the specification does not enable a method of immunization. If the Examiner admits that

the invention will induce an immune response, why does the specification not enable a method of immunization?

With regard to the assertions on page 8 of Paper No. 22 that "immunization" is limited to a meaning of providing protection to an individual, this is incorrect. The specification teaches on page 16, lines 16-26, that the invention (i.e., inducing an immune response) may provide a treatment (e.g., immunoprotection, desensitization, immunosuppression, modulation of autoimmune disease, potentiation of cancer immunosurveillance, or therapeutic vaccination against an established infectious disease). The antigen-specific immune response induced by transcutaneous immunization may be used to provide a protective immune response for prophylactic or therapeutic treatment. For example, vaccination would be expected to induce its prophylactic or therapeutic effects through humor immunity (e.g., antibody) and/or cellular immunity (e.g., CTL lysis). Prophylactic and/or therapeutic treatment is a preference; it is not a requirement (page 9, lines 24-25, and page 10, lines 17-27, of the specification). All that is required is that at least one antigen-specific component of the humoral and/or cellular immune system is induced (see page 37, lines 13-15, of the specification). The Examples of the present specification clearly illustrate that production of antigen-specific antibody, CTL lysis, and cell proliferation are sufficient to show that an immune response was induced.

Sequestrin is not the only antigen which may be used in genetic transcutaneous immunization. Examples 19 and 20 show that both polynucleotide and protein forms of sequestrin antigen will induce an antigen-specific immune response when antigen is applied epicutaneously. This is merely illustrative of the invention and no reasons are given in the Office Action to contradict the objective truth of Applicants' teaching that a variety of antigens would be effective. Similarly, a regulatory region is not required to practice the invention. Examples 34 and 38 show that CpG1 is an effective adjuvant which does not require a regulatory region to produce a protein encoded by the polynucleotide.

Although the Patent Office has not sustained its burden to provide "evidence or reasoning which is inconsistent with the contested statement," Applicants have cited working examples which show that the claims should not be limited in the manner

proposed by the Examiner. There has been no evidence or reasoning presented which is inconsistent with the Applicants' teachings. Inducing an immune response requires that antigen-specific components of the immune system be produced. This is shown by the working examples of the specification.

The references Ockenhouse et al. and McCluskie et al. cited in the Office Action are not probative of whether undue experimentation would be required to practice the claimed invention because they are not concerned with transcutaneous immunization. Ockenhouse et al. teach that sequestrin is a good candidate for a vaccine component. It is the Examiner's speculations about the difficulty of preparing a vaccine and the failure of others who have not used transcutaneous immunization from which he concludes that the *Wands* factors support a prima facie case of nonenablement. But even if the Examiner's conclusion is accepted for the sake of argument, it does not show that other antigens, which have been used as a vaccine component (e.g., diphtheria toxoid), would not be usefully delivered by transcutaneous immunization. McCluskie et al. inject DNA vaccines. Therefore, their failure is not relevant here because injection is outside the scope of the claimed invention and they do not appreciate the advantage of delivering antigen via transcutaneous immunization. Moreover, and as explained above, it should be noted that Applicants' invention is not limited to vaccines and providing a medical treatment. Transcutaneous immunization is a general methodology for inducing an immune response and such includes utilities which do not require prophylaxis or therapy (e.g., immunoassay for detection of antigen and diagnosis of infection).

Finally, claim 24 of U.S. Patent 6,310,046 demonstrates that it does not require undue experimentation to use sequestrin DNA for genetic immunization by different routes (i.e., intramuscular, intradermal, or intranasal administration). If this rejection is maintained, Applicants request that the next Office Action explain what teaching in the '046 patent leads to the conclusion that claim 24 is enabled and how is this teaching lacking in the present specification.

Withdrawal of the enablement rejection made under Section 112, first paragraph, is requested because it would not require undue experimentation for a person of skill in the art to make and use the claimed invention.

Conclusion

Having fully responded to all of the pending objections and rejections contained in the Office Action (Paper No. 22), Applicants submit that the claims are in condition for allowance and earnestly solicit an early Notice to that effect. The Examiner is invited to contact the undersigned if any further information is required.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: _____

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Attachments: U.S. Patent 5,910,306; U.S. Patent 5,980,898; U.S. Patent 6,310,046; and WO 98/20734